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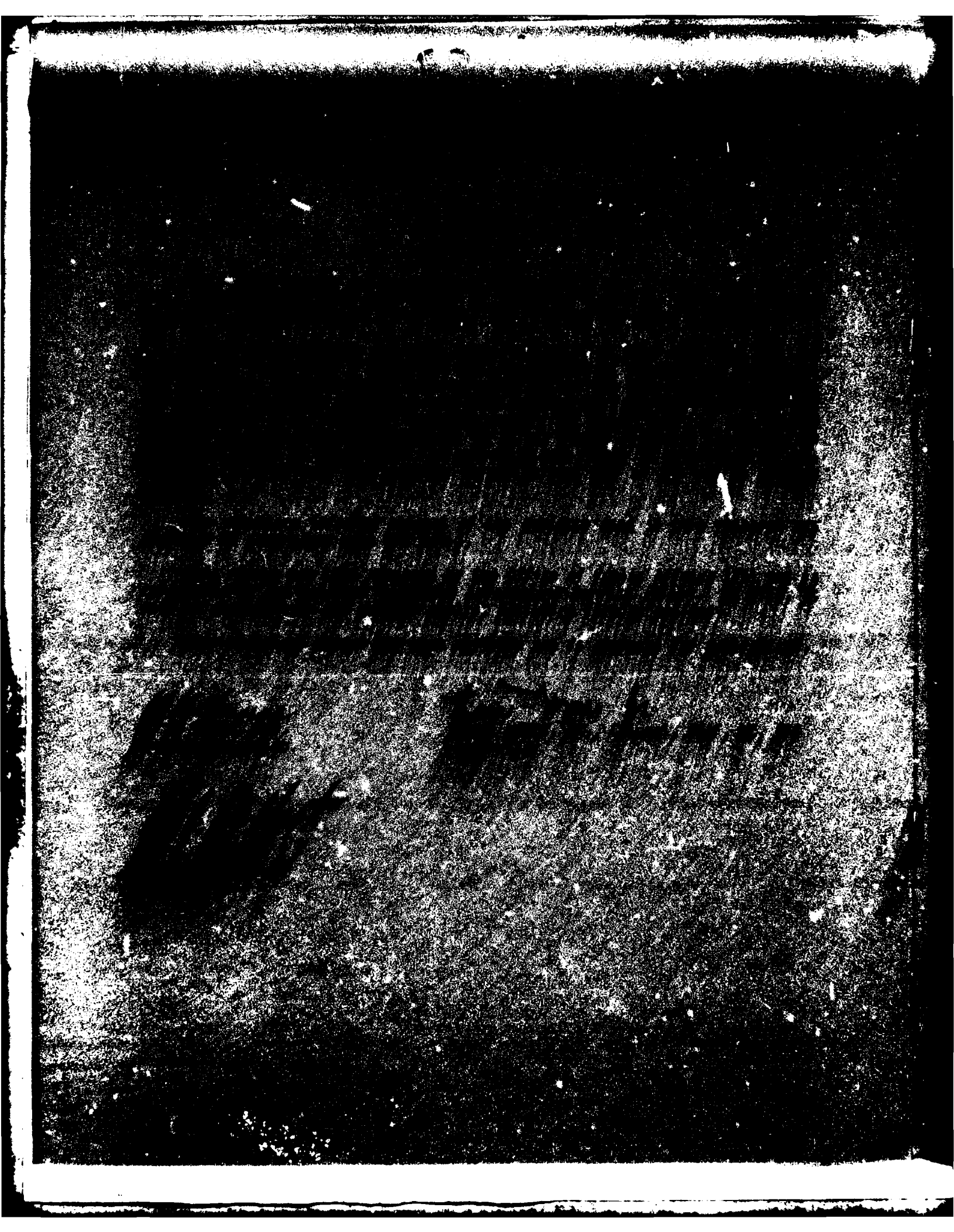
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) A prospective study to investigate the reported association of earlobe crease with coronary artery disease was carried out in 1172 largely asymptomatic male patients medically evaluated to determine fitness to fly. A subset of 172 men had coronary angiography and 28% were found to have coronary artery disease. We found a strong statistical association between earlobe creases and age, in both our total group of 1172 patients and the 172 who had coronary angiography. We conclude that the earlobe crease is associated with age		

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20. ABSTRACT (Continued)

and age is strongly associated with coronary artery disease; but, after removing the effect of age, earlobe creases do not further improve the prediction of coronary artery disease.

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EARLOBE CREASE AND CORONARY ARTERY DISEASE

INTRODUCTION

In 1965 VerNooy (1) reported a significant association between earlobe creases and myocardial infarctions; however, coronary angiography was not generally available at that time and actual vessel status was not determined. In 1973 Frank (2) reported a definite correlation between "a prominent crease in the lobule portion of the auricle" and premature cardiovascular disease and suggested that further evaluation of this relationship was warranted. In 1974 Lichstein et al. (3) reported an increased incidence of "diagonal earlobe crease" in postinfarction patients, but no angiographic data was cited. Subsequently, three additional papers (4, 5, 6) in support of this presumed association were published, but all were based on clinical data rather than angiography.

Later, in 1974, Mehta and Hamby (7) reported the first study based on coronary arteriography; they concluded that the crease was more likely associated with age rather than coronary artery disease (CAD). Sternlieb et al. (8) then reported on 144 patients who had coronary angiography and claimed it to be the first study showing a relationship between CAD and ear creases. In September 1976 Lichstein et al. (9), based on postmortem study of 113 patients, found a significant difference in the prevalence of coronary sclerosis in the no-crease group compared with the bilateral crease group, with inconclusive results in those with a unilateral crease. In August 1977 Frank (10) reported two patients with classic angina and earlobe creases who had normal coronary arteriograms; he suggested that they might have "small vessel disease." Kaukola (11), in 1978, based on coronary angiography in 286 patients, strongly supported the findings of Sternlieb et al. (8). In August 1979 Haft et al. (12) reported 445 patients who had coronary arteriography. When this group was divided according to age by 20-year periods, there was no significant difference in any age group between those with CAD and those with normal coronaries.

METHODS AND MATERIALS

The study group was accumulated in a prospective manner and consisted of male patients who were evaluated at the USAF School of Aerospace Medicine (USAFSAM) Aeromedical Consultation Service during the study period. Over 95% of the patients had no history or symptom of overt cardiovascular disease. They were apparently healthy USAF flyers who were referred for medical evaluation because of a finding such as nonspecific T wave changes on a routine ECG or because of an event, such as syncope, that raised the question of medical qualification for flying duties. Every patient had a complete medical evaluation which included a resting standard 12-lead ECG, Frank-lead vectorcardiogram, and maximal treadmill exercise stress test using the Balke protocol. If clinically indicated, patients had additional special studies, such as phonocardiography, apexcardiography, echocardiography, or radionuclide myocardial imaging. Individuals who had either supraventricular tachycardia, acquired

bundle branch block, or an abnormal electrocardiographic response to maximal treadmill testing, and who were otherwise fit for flying duties, were offered a left heart catheterization with selective coronary angiography in multiple projections.

Photographic documentation of the appearance of the ear was elected to reduce reader bias by other risk factors for coronary artery disease and to assess between- and within-reader consistency. A Nikkormat camera fitted with a 55 mm lens and a ring flash was used. All subjects were photographed in the seated posture. Subjects who underwent coronary angiography were photographed prior to cardiac catheterization.

A total of 1172 male patients had satisfactory photographs taken between April 1975 and June 1979, and 172 had coronary angiography.

To determine any possible significance of earlobe shape and crease angle, 704 earlobe photographs on 352 subjects were read independently by two authors (HHH and MCL), and each was coded as to earlobe shape, whether an observed crease descended vertically or at an angle, and whether an observed crease was shallow, was deep but did not extend through the earlobe margin, or was deep and extended through the margin. All of the photographs of the 1172 patients were read in this manner by one author (HHH). The results of these readings were then compared between readers for each of the earlobe characteristics. There was between-reader disagreement approximately 25% of the time regarding both shape of earlobe and angle of a crease. We felt that scoring the shape of the earlobe and the angle of a crease was not sufficiently consistent to warrant further investigation. Between-reader disagreement was only 7% for the presence/absence of any crease and 3% for the scoring of crease depth.

Of the 352 subjects scored by two of us (HHH and MCL), 125 had coronary angiography. Without divulging the angiographic findings of any individual subject, one of us (WGJ), who was not involved in the interpretation of photographs, found no association of coronary angiography scores with any measure of earlobe crease in these 125 subjects after controlling for age. Concerned that we had not read our photographs with the same criteria that were used by other authors who reported an association between "significant" creases and angiographically proven coronary artery disease, a contributor to each of three previously published articles, which were based on angiography, was contacted (7, 8, 11). All very kindly agreed to interpret 32 photographs of 16 subjects (none of whom had cardiac catheterization) for the presence or absence of "significant" creases. The three of us also independently read these 32 ears for a total of six interpretations. These 32 photographs were selected to represent the spectrum of earlobe creases with special attention to borderline examples. These 32 photographs were not a random sample of all earlobe creases. After reviewing the responses from the independent scoring of the three authors, it was not possible to state what constituted a "significant" earlobe crease. These three authors were as likely to score a vertical crease as being "significant" as they were an angular crease. The three authors disagreed on 8 of the 32 ears, and no two of them were in better agreement. Even using the majority rule in the 8 disputed ears, we were unable to define, in words, criteria for a "significant" earlobe crease. When combined with our scoring, disagreement on 15 of the 32 ears was found. In particular, we were unable to define criteria such that when we interpreted the 15 disputed photographs, we improved our within- or between-reader agreement. Keeping in mind those

photographs upon which all agreed, three of us (HHH, MCL, GDT) then independently read the photographs on only those subjects who had coronary angiography. By this point in the study, that number had increased to 172 subjects. Figure 1 shows samples of what the three of us agreed were lobes without any crease, lobes with insignificant creases, and lobes with significant creases.

The coronary angiograms were interpreted independently by a minimum of two cardiologists who were not involved in this study. All equivocal or contradictory interpretations were resolved by a third interpreter and a conference of readers. Coronary angiograms were classified into three categories: normal (judged to be completely free of any luminal obstruction or intimal roughening); <50% (evidence of luminal obstruction(s) with the maximum diameter narrowing less than 50%); and >50% (at least one lesion with a 50% or greater obstruction).

After the three of us had independently scored the photographs of the 172 subjects, the angiographic data were tested for an association with earlobe findings. It is important to emphasize that the readers had no knowledge of the angiographic findings at the time the photographs were scored for the presence or absence of earlobe crease.

RESULTS

The prevalence of any earlobe crease, as judged by each of us, is presented in Table 1 according to coronary angiographic findings in our 172 patients. The subjective evaluation as to whether or not the patient had a "significant" earlobe crease is shown in Table 2. Interobserver variation concerning presence or absence of any earlobe crease had no significant effect on the results.

TABLE 1. INDEPENDENT INTERPRETER SCORING FOR ANY CREASE IN 172 CATHETERIZED SUBJECTS

Interpreter	Crease	Angiography		
		<u>≥ 50%</u>	< 50%	Normal
HHH	+	18	6	59
	-	15	10	64
MCL	+	18	6	56
	-	15	10	67
GDT	+	19	6	51
	-	14	10	72

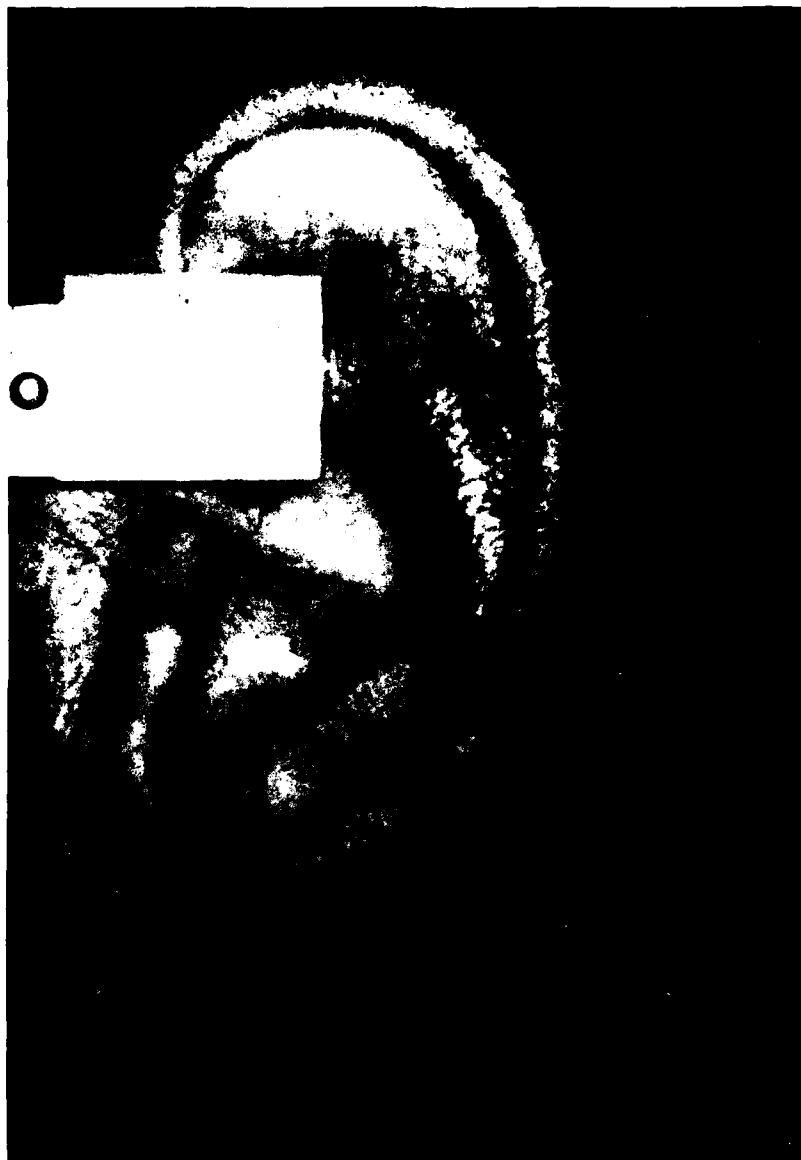


Figure 1A. Rudimentary earlobe with a fine facial crease but no earlobe crease.

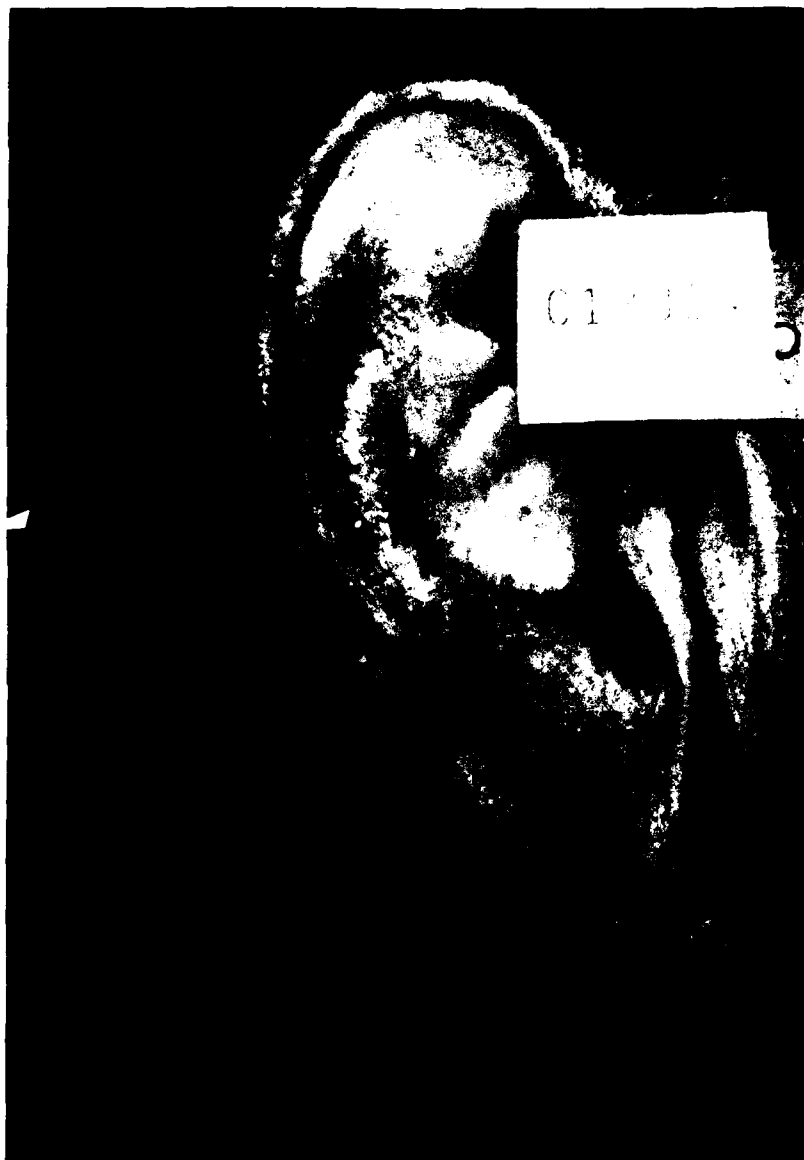


Figure 1B. Well-formed, dependent earlobe with a prominent facial crease but no earlobe crease.



Figure 1C. A shallow, diagonal crease through the margin, scored insignificant.



Figure 1D. A shallow, short crease from the helical fold to the margin, scored insignificant.

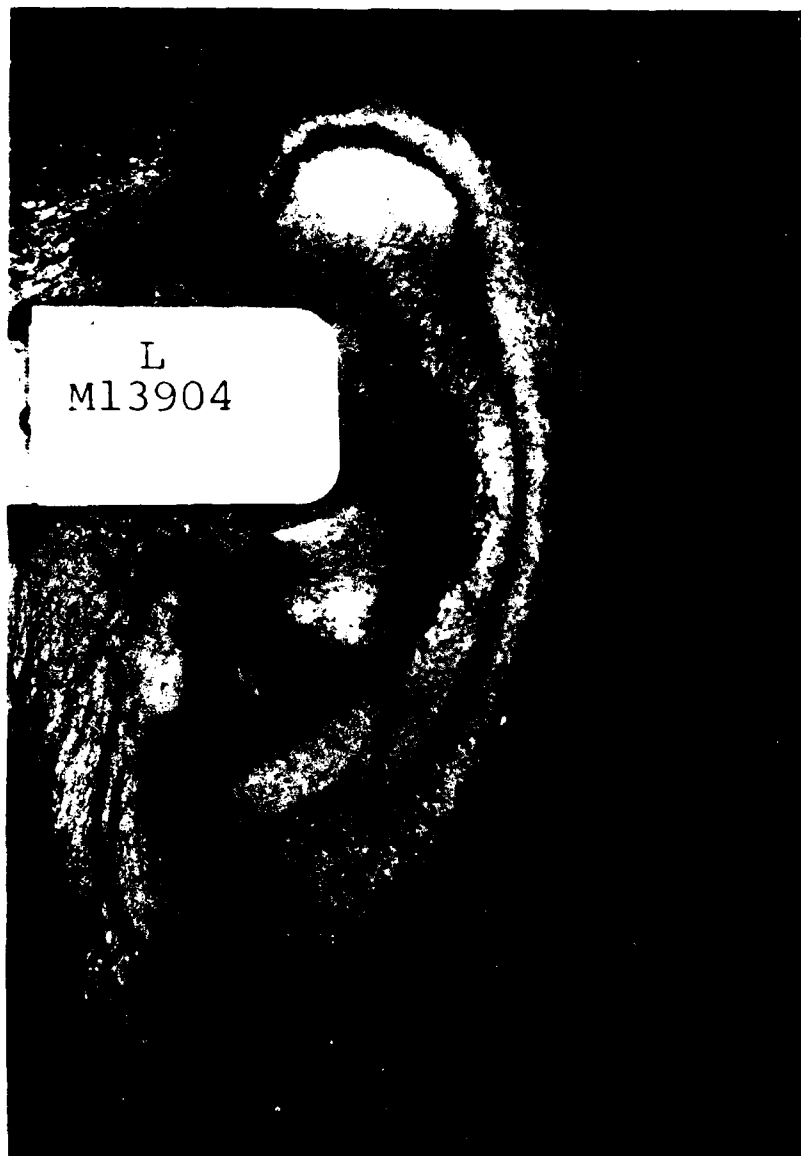


Figure 1E. A deep vertical crease through the margin, scored significant.

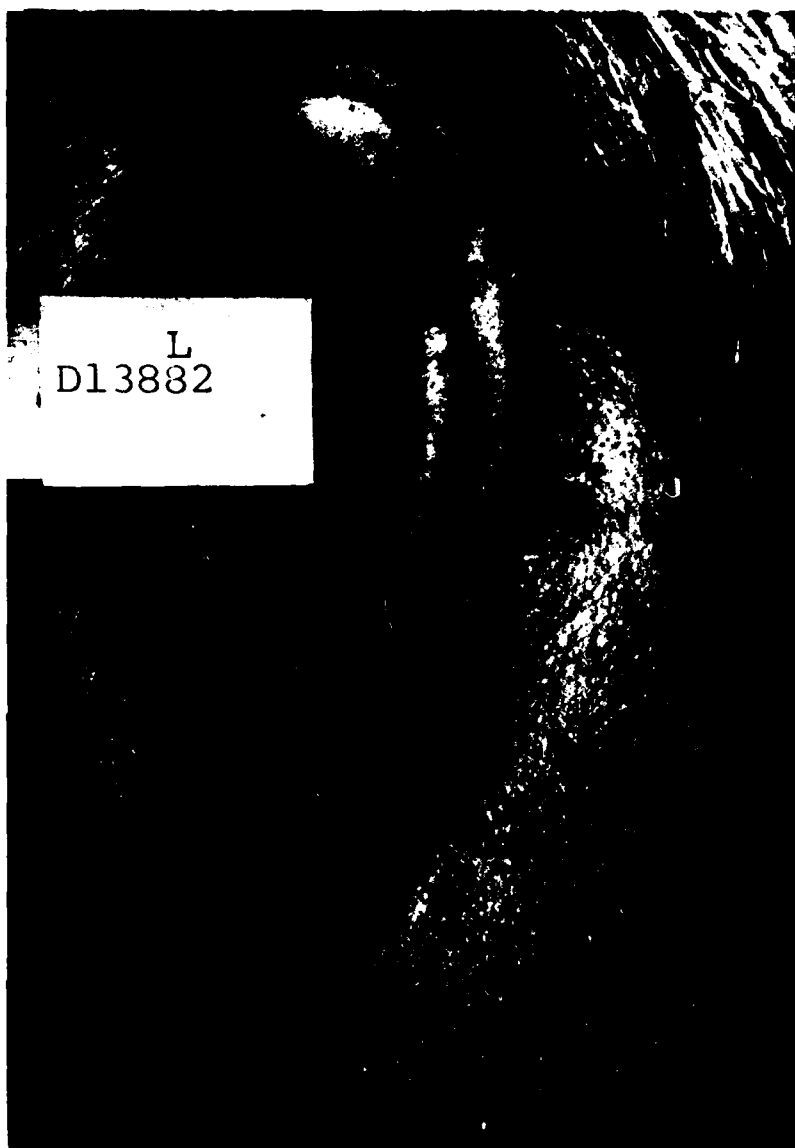


Figure 1F. A deep diagonal crease which does not extend to the margin, scored significant.

TABLE 2. INDEPENDENT INTERPRETER SCORING FOR SIGNIFICANT CREASES IN 172 CATHETERIZED SUBJECTS

Interpreter	Crease	Angiography		
		$\geq 50\%$	$< 50\%$	Normal
HHH	+	12	2	23
	-	21	14	100
MCL	+	10	3	25
	-	23	13	98
GDT	+	10	2	36
	-	23	14	87

There was a clear and striking association between age and the presence of an earlobe crease in the 1172 individuals photographed and in the subset of 172 individuals who underwent coronary angiography, as shown in Figure 2. An age-crease association can be seen for each interpreter in Table 3. When the patients were separated according to presence of unilateral or bilateral creases in the entire group of 1172, an association between age and both unilateral and bilateral creases was also seen.

The association between earlobe crease and coronary artery disease was tested after adjusting for age by the multidimensional contingency table method (13). Results are shown in Table 4. This analysis is based on the interpretation by HHH as shown in Table 5. There was no significant association between earlobe creases and coronary artery disease after adjusting for age. There was a strong association of coronary artery disease with age ($p < .0005$) and also of earlobe creases with age ($p < .0001$).

DISCUSSION

Rhoads (14, 15) and co-workers have very appropriately pointed out the lack of a specific definition for what constitutes a "significant" earlobe crease. Haft et al. (12), Rhoads et al. (14), and Kaukola (11) made attempts to define what they classified as a significant crease, but we found many examples that could not be classified consistently by any of their criteria. We also had difficulty establishing criteria with words; however, by using examples we achieved results that are not dependent upon who did the classification.

Our study population had a number of differences from other reported series. First, it was generally younger than other series, with 93.3% of our 1172 patients under age 50 and 94.2% of our 172 patients who had coronary angiography under age 50. It was not always possible to directly compare the

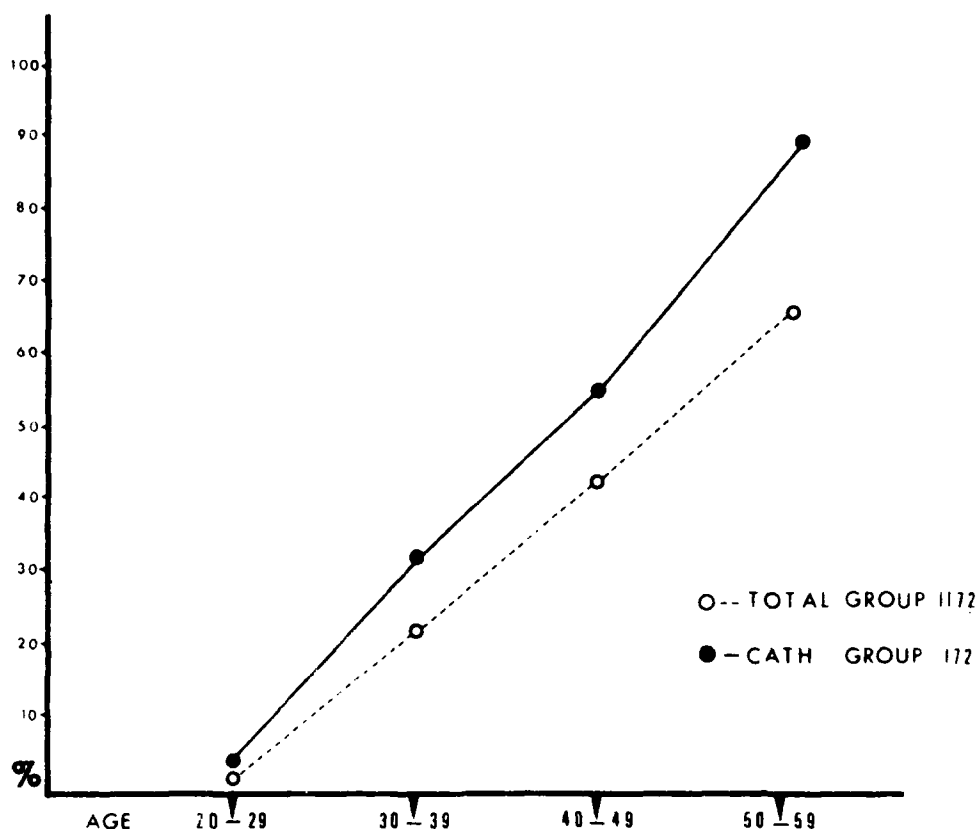


Figure 2. Age vs crease in the USAFSAM study group and the total population photographed (including the study group), based on interpretation of HHH.

ages of our subjects to that of other study groups because insufficient data was presented in several series. However, only 57.3% of Kaukola's (11) patients who underwent coronary angiography were under 50 years of age. Sternlieb et al. (8) reported a mean age of 56 years for his patients; in the group reported by Haft et al. (12) 69% of the men and 86% of the women were ≥ 40 years old. In the study by Christiansen et al. (4) 85.3% of the total group were ≥ 50 years old, while 99.4% of the coronary disease group and 75% of the control group were ≥ 50 years old. Second, our population of 1172 is different in selection. These patients were referred for evaluation usually because of a finding which possibly could be waived for flying duties. However, since these patients were asymptomatic, apparently healthy men actively pursuing full-time careers as Air Force flyers until discovered to have some problem on routine periodic physical examination, differences in our subjects from the general American male population should be less than in patients hospitalized for symptoms or myocardial infarction or examined at autopsy. Even so, our catheterized group cannot be considered a random sample of the general population since 28% had angiographically proven coronary artery

TABLE 3. OCCURRENCE OF ANY CREASE WITHIN AGE GROUPINGS BY ANGIOGRAPHIC RESULTS FOR EACH INTERPRETER (N=172)

Interpreter	Age	Crease	Angiography		
			$\geq 50\%$	$< 50\%$	Normal
HHH	20-29	+			1
		-		1	10
	30-39	+		1	15
		-	3	2	29
	40-49	+	16	5	37
		-	11	7	24
	50-59	+	2		6
		-	1		1
M.L.	20-29	+			1
		-		1	10
	30-39	+		1	14
		-	3	2	30
	40-49	+	16	5	35
		-	11	7	26
	50-59	+	2		6
		-	1		1
GDT	20-29	+			1
		-		1	10
	30-39	+	1	2	12
		-	2	1	32
	40-49	+	15	4	33
		-	12	8	28
	50-59	+	3		5
		-			2

TABLE 4. PARTIAL ASSOCIATION BETWEEN ANGIOGRAPHICALLY PROVEN CORONARY DISEASE, AGE, AND CREASE (172 SUBJECTS). THIS IS ASSOCIATION BETWEEN TWO FACTORS ADJUSTED FOR THE THIRD. RESULTS ARE EAG ON TABLE 5.

Partial association	Degrees of freedom	Likelihood ratio chi-square	Probability
CAD with creases	2	1.86	0.39
CAD with age	4	20.75	0.0004
Creases with age	2	19.20	<0.0001

TABLE 5. FREQUENCY TABLE UPON WHICH TABLE 4 WAS COMPUTED. PRESENCE OR ABSENCE OF CREASES BASED ON INTERPRETATION BY HHH.

Age	Crease	Angiography		
		$\geq 50\%$	$< 50\%$	Normal
≤ 39	+	0	1	16
	-	3	3	39
40-44	+	9	2	28
	-	6	6	20
≥ 45	+	9	3	15
	-	6	1	5

disease. Third, the indication for coronary angiography in our 172 subjects was to determine fitness for flying duties, and not for the presence of symptoms. Fourth, all of the previously published studies had a very high disease prevalence, i.e., 84% in the Sternlieb et al. (8) study, 75% in the study by Mehta and Hamby (7), 70% in Kaukola's study (11), and 69% in the study by Haft et al. (12). In contrast, the disease prevalence in our angiography group was 28%. Fifth, there were marked differences in the prevalence of creases between studies.

Rhodes et al. (14, 15) emphasized the lack of consistency in the published data with respect to the significance of earlobe creases, the possibility for bias in the studies, and the selective nature of the populations reported. Haines (16), in analyzing the data of Lichstein et al. (3), made the obvious point that if the prevalence of earlobe creases was applied to a population with a low prevalence of disease, an unacceptably high false-positive rate would be experienced. Later, Haft et al. (12) followed Haines' example and calculated that a false-positive rate of 83% would be experienced using their data applied to a population with 10% prevalence of disease. Thus, these authors emphasized the importance of disease prevalence in a study population.

We reviewed the published studies (7, 8, 11, 12) in which coronary angiography was employed to determine the presence or absence of coronary artery disease, and we calculated the sensitivity, specificity, predictive value, odds ratio, and prevalences of disease and creases for each study. The results are presented in Table 6, along with the expected values (in parentheses) under the null hypothesis that no association exists. The statistics were computed without an adjustment for age, since the necessary information to do this was not available for all the studies. It should be noted that the statistics are all influenced by the underlying age distributions, and only the odds ratio avoids effects of differing disease prevalence and varying definitions of disease between studies.

As can be seen in Table 6, the study by Sternlieb et al. (8) had the greatest difference from the others with a sensitivity of over 99%, a predictive value of 90%, and an odds ratio of 92.3. Although their data has some small cell sizes, adding two or three more observations to the smallest cell would still leave the data showing a very strong association. The other studies show lower odds ratios, with Kaukola's study (11) having the next largest value at 9.7. Our data with an odds ratio of 1.04 agree with the study of Mehta and Hamby (7), which shows a lack of association between the earlobe crease and coronary artery disease.

Both Mehta and Hamby (7) and Haft et al. (12) reported a positive association between earlobe creases and age. Kaukola (11) stated that the increase in earlobe crease prevalence with age was not statistically significant in the patients with coronary artery disease nor in those without coronary artery disease; however, when we analyzed the data on the group studied by coronary angiography, we found a very strong association of earlobe crease with age, which was statistically significant ($p < .0001$). Our study also showed a strong association between earlobe creases and age ($p < .0001$). After adjusting for age, we found no association between the presence of any earlobe crease or coronary artery disease. We suspect that the reports of a positive association between earlobe creases and coronary artery disease are due to failure to adjust for age.

TABLE 6. COMPARISON OF PUBLISHED AND USAFSAM DATA BASED ON CORONARY ANGIOGRAPHY. (NUMBERS IN PARENTHESES ARE EXPECTED VALUES ASSUMING NO CREASE-DISEASE ASSOCIATION, IGNORING AGE.)

Investigators	No.	Crease	CAD	Normal	Sensitivity	Specificity	Predictive value	Odds ratio	CAD prevalence	Crease prevalence
Mehta and Hamby (1974)	211	+	89	26	56% (55%)	50% (45%)	77% (75%)	1.3 (1.0)	75%	55%
Sternlieb et al. (1974)	144	+	120	13	99% (92%)	43% (8%)	90% (84%)	92.3 (1.0)	84%	92%
Kaukola (1978)	286	+	144	18	72% (57%)	79% (43%)	89% (70%)	9.7 (1.0)	70%	57%
Haft et al. (1979)	445	+	159	33	52% (43%)	76% (57%)	83% (69%)	3.5 (1.0)	69%	43%
USAFSAM	172	+	24	59	49% (48%)	52% (52%)	29% (28%)	1.04 (1.0)	28%	48%

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